

-51-

Step E: Acylation of the primary amine

6-Amino-2-(4-but-2-yloxy-phenylsulfanyl)-hexanoic acid hydroxyamide resin prepared in Step D (0.33 g, 1.1 meq/g) was suspended in DMF (60 mL). N-Phthaloyl glycine (1.5 g, 4.0 eq.) 1-hydroxybenzotriazole hydrate (HOBt, 1.43 g, 6.0 eq.) and 1,3-diisopropyl-carbodiimide (DIC, 0.18 mL, 4.0 eq.) were added. The reaction was shaken on an orbital shaker at room temperature for 2 - 16 hours. The reaction was filtered and washed with DMF (3 x 5 mL). A sample of resin was removed and subjected to the Kaiser test. If the test showed the presence of free amine (resin turned blue) the coupling described above was repeated, otherwise the resin was washed with DCM (3 x 5 mL), MeOH (2 x 5 mL), and DCM (2 x 5 mL). The resin was dried *in vacuo* at room temperature.

Step F: Cleavage of 2-(4-but-2-yloxy-phenylsulfanyl)-6-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-acetylamino]-hexanoic acid hydroxyamide from the resin

The 2-(4-but-2-yloxy-phenylsulfanyl)-6-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-acetylamino]-hexanoic acid hydroxyamide resin prepared in Step E (0.33g, 1.1 meq/g) was suspended in DCM (1.0 mL) and TFA (1.0 mL) was added. The reaction was shaken for 1 hour at room temperature. The reaction was filtered and the resin washed with DCM (2 x 1 mL). The filtrate and the washing were combined and concentrated to dryness on a Savant SpeedVac Plus. Methanol (1 mL) was added and the mixture concentrated.

The crude product was purified by reverse phase HPLC under the following conditions:

benzenesulfonic acid (2 g) were added. The reaction mixture was shaken on an orbital shaker at room temperature for 12 - 24 hours. The reaction was filtered and washed with DCM (2 x 50 mL), DMF (2 x 50 mL), MeOH (2 x 50 mL), and DCM (2 x 50 mL). The resin was dried *in vacuo* at room temperature.

5

Step B: Removal of the phthaloyl group

2-(4-But-2-ynoxy-benzenesulfinyl)-6-phthaloyl hexanoic acid hydroxyamide resin prepared in Step A was deprotected to give 6-amino-2-(4-but-2-ynoxy-benzenesulfinyl)-hexanoic acid hydroxyamide resin according to the procedure in
10 **Example 13, Step D.**

Step C: Acylation of the primary amine

6-Amino-2-(4-but-2-ynoxy-benzenesulfinyl)-hexanoic acid hydroxyamide resin (0.33 g, 1.1 meq/g) prepared in step B was acylated with quinaldic acid (1.2 g, 4.0 eq) according to the procedure in **Example 13, Step E** to give quinoline-2-carboxylic acid [5-(4-but-2-ynyloxy-benzenesulfinyl)-5-hydroxycarbamoyl-pentyl]-amide resin.
15

Step D: Cleavage of quinoline-2-carboxylic acid [5-(4-but-2-ynyloxy-benzenesulfinyl)-5-hydroxycarbamoyl-pentyl]-amide from the resin
20

Quinoline-2-carboxylic acid [5-(4-but-2-ynyloxy-benzenesulfinyl)-5-hydroxycarbamoyl-pentyl]-amide resin prepared in Step C (0.33g, 1.1 meq/g) was cleaved according to the procedure in **Example 13, Step F** to give **Example 23**: quinoline-2-carboxylic acid [5-(4-but-2-ynyloxy-benzenesulfinyl)-5-hydroxy-carbamoyl-pentyl]-amide as a mixture of diastereomers which had HPLC retention time² 4.35/4.5 min. and MS³ 494 (M+H).
25

The following hydroxamic acids compounds are synthesized following the steps in **Example 23**, and using N-phthaloyl glycine, 2-benzylcarboxylic acid, 3,4-dichlorophenylacetic acid, 3-quinoline carboxylic acid, 4-(2-thienyl)butyric acid,
30